[0069] In addition, certain hypocretin polypeptides derived from receptor binding portions of hypocretin have the capacity to inhibit the binding of the hypocretin that would normally bind a hypocretin receptor. Thus, the invention also includes hypocretin polypeptides which are specifically designed for their capacity to mimic exposed regions of hypocretin involved in hypocretin receptor binding interactions and thereby receptor function. Therefore, these polypeptides have the capacity to function as analogs to hypocretin, and thereby block function.

[0070] In addition, polypeptides corresponding to exposed domains have the ability to induce antibody molecules that immunoreact with a hypocretin of this invention at portions of hypocretin involved in receptor protein function, and therefor the antibodies are also useful at modulating normal hypocretin function.

[0071] A hypocretin polypeptide is preferably no more than about 120 amino acid residues in length for reasons of ease of synthesis. Thus, it more preferred that a hypocretin polypeptide be no more that about 100 amino acid residues, still more preferably no more than about 50 residues, and optimally less than 40 amino acid residues in length when synthetic methods of production are used. Exemplary polypeptides are hcrt1 and hcrt2.

[0072] The present invention also includes a hypocretin polypeptide that has an amino acid residue sequence that corresponds to the sequence of the hypocretin protein shown in the sequence listings, and includes an amino acid residue sequence represented by a formula selected from the group consisting of the polypeptides shown in the sequence listings. In this embodiment, the polypeptide is further characterized as having the ability to mimic a hypocretin epitope and thereby inhibits hypocretin function in a classic hypocretin receptor activation assay, as described herein.

[0073] Due to the three dimensional structure of a native folded hypocretin molecule, the present invention includes that multiple regions of hypocretin are involved in hypocretin receptor function, which multiple and various regions are defined by the various hypocretin polypeptides described above, A preferred hypocretin receptor ligand is hcrt. The ability of the above-described polypeptides to inhibit receptor-ligand binding can readily be measured in a ligand binding assay as is shown in the Examples herein. Similarly, the ability of the above-described polypeptides to inhibit hypocretin receptor function can readily be measured in a receptor assay as is described herein.

[0074] In another embodiment, the invention includes hypocretin polypeptide compositions that comprise one or more of the different hypocretin polypeptides described above which inhibit hypocretin receptor function, admixed in combinations to provide simultaneous inhibition of multiple contact sites on the hypocretin receptor.

[0075] A subject polypeptide includes any analog, fragment or chemical derivative of a polypeptide whose amino acid residue sequence is shown herein so long as the polypeptide is capable of mimicking an epitope of hypocretin. Therefore, a present polypeptide can be subject to various changes, substitutions, insertions, and deletions where such changes provide for certain advantages in its use. In this regard, a hypocretin polypeptide of this invention corresponds to, rather than is identical to, the sequence of a hypocretin protein where one or more changes are made and it retains the ability to induce antibodies that immunoreact with a hypocretin of this invention.

[0076] The term "analog" includes any polypeptide having an amino acid residue sequence substantially identical to a sequence specifically shown herein in which one or more residues have been conservatively substituted with a functionally similar residue and which displays the ability to induce antibody production as described herein. Examples of conservative substitutions include the substitution of one non-polar (hydrophobic) residue such as isoleucine, valine, leucine or methionine for another, the substitution of one polar (hydrophilic) residue for another such as between arginine and lysine, between glutamine and asparagine, between glycine and serine, the substitution of one basic residue such as lysine, arginine or histidine for another, or the substitution of one acidic residue, such as aspartic acid or glutamic acid for another.

[0077] The phrase "conservative substitution" also includes the use of a chemically derivatized residue in place of a non-derivatized residue provided that such polypeptide displays the requisite binding activity.

[0078] "Chemical derivative" refers to a subject polypeptide having one or more residues chemically derivatized by reaction of a functional side group. Such derivatized molecules include for example, those molecules in which free amino groups have been derivatized to form amine hydrochlorides, p-toluene sulfonyl groups, carbobenzoxy groups, t-butyloxycarbonyl groups, chloroacetyl groups or formyl groups. Free carboxyl groups may be derivatized to form salts, methyl and ethyl esters or other types of esters or hydrazides. Free hydroxyl groups may be derivatized to form O-acyl or O-alkyl derivatives. The imidazole nitrogen of histidine may be derivatized to form N-im-benzylhistidine. Also included as chemical derivatives are those peptides which contain one or more naturally occurring amino acid derivatives of the twenty standard amino acids. For examples: 4hydroxyproline may be substituted for proline; 5-hydroxylysine may be substituted for lysine; 3-methylhistidine may be substituted for histidine; homoserine may be substituted for serine; and ornithine may be substituted for lysine. D-amino acids may also be included in place of one or more L-amino acids. Polypeptides of the present invention also include any polypeptide having one or more additions and deletions or residues relative to the sequence of a polypeptide whose sequence is shown herein, so long as the requisite activity is maintained.

[0079] The term "fragment" refers to any subject polypeptide having an amino acid residue sequence shorter than that of a polypeptide whose amino acid residue sequence is shown herein.

[0080] When a polypeptide of the present invention has a sequence that is not identical to the sequence of a hypocretin polypeptide, it is typically because one or more conservative or non-conservative substitutions have been made, usually no more than about 30 number percent, more usually no more than 20 number percent, and preferably no more than 10 number percent of the amino acid residues are substituted. Additional residues may also be added at either terminus for the purpose of providing a "linker" by which the polypeptides of this invention can be conveniently affixed to a label or solid matrix, or carrier. Preferably the